REMARKS

Amendments to the Claims

Claims 1-6, 8-10 and 12-16 are pending. The Applicants respectfully ask the Examiner to replace all prior versions and listings of claims in the present application with the listing of claims currently provided. Claims 1-3, 5, 6, 8-10, and 12-16 were amended; and Claims 17-27 are new. The Applicants hereby state that all amendments do not add new subject matter to the specification.

Amendment support for Claims 1 and 12 can be found at, *e.g.*, pg. 20, lines 7-10; pg. 21, lines 5-8; pg. 21, lines 13-14; pg. 33, lines 26-27; pg. 39, lines 25-31; and Examples 2 and 3.

Amendment support for Claims 2, 3, 13, 14, 26 and 27 can be found at, *e.g.*, pg. 4, lines 12-15; pg. 19, lines 29-32; and pg. 23, lines 7-9.

Amendment support for Claims 5 and 19 can be found at, *e.g.*, pg. 6, lines 21-24; pg. 12, lines 2-31; pg. 20, lines 7-10; pg. 21, lines 5-8; pg. 31, lines 22-25; pg. 36, lines 25-28; pg. 39, lines 25-31; and Example 1.

Amendment support for Claim 6 can be found at, *e.g.*, pg. 2, lines 27-29.

Amendment support for Claims 17 and 18 can be found at, *e.g.*, pg. 2, lines 4-11.

Amendment support for Claims 22-24 can be found at, *e.g.*, pg. 1, lines 19-23.

Amendment support for Claim 25 can be found at, *e.g.*, pg. 19, lines 17-20; pg. 21, lines 20-22; pg. 22, lines 26-29; pg. 23, lines 7-9; pg. 36, lines 25-28; and Example 4.

Rejection Pursuant to 35 U.S.C. § 102(e) Anticipation

The Examiner has rejected Claims 1-5 and 12 as allegedly being anticipated under 35 U.S.C. § 102(e) by Sung-Yun Kwon, *Solid Solution Perforator for Drug Delivery and Other Applications*, U.S. Patent Application 2004/0087893 (May 6, 2004), hereafter the "Kwon publication," as evidenced by BOTOX® Therapeutic package insert, Allergan, Inc., Irvine, CA (2004), hereafter the "Allergan therapeutic insert." The Applicant respectfully asks for reconsideration under 37 C.F.R. §1.111.

Present independent Claim 1 and its dependent Claims 2-6, 8-10, 17 and 18 are directed, in part, towards a method of treating a skin disorder by administering a liquid solution comprising a botulinum toxin by intradermal injection or subdermal injection. Present independent Claim 12 and its dependent Claims 13-16 and 19-24 are directed, in part towards, a method of treating a skin disorder by administering a liquid solution comprising a botulinum toxin by intradermal injection or subdermal injection. Present independent Claim 25 and its dependent Claims 26 and 27 are directed, in part, towards a method of treating a skin disorder by topically administering a cream or a lotion composition comprising a botulinum toxin.

According to *MPEP* § 2131, for a reference to anticipated a pending claim, that reference must teach each and every element of the pending claim.

I. The Kwon publication does not disclose administering a liquid solution.

The Examiner asserts that the Kwon publication discloses a method of administering a safe and effective amount of botulinum toxin type A for "treating lesions or abnormal skin features, such as pimples, corns, warts, calluses, bunions and keratoses." March 22, 2007 Office Action at pg. 3, ¶ 3, line 1-4.

The Kwon publication discloses a solid drug solution perforator (SSP) device for the delivery of a therapeutic, prophylactic or cosmetic compound. See, *e.g.*, abstract, lines 1-3. The SSP device comprises, in part, an array of one or more solid perforators composed of a matrix material and drug and an activatable pressure mechanism. See, *e.g.*, ¶ 10, lines 1-9; and

Claim 1. The matrix biodegrades or dissolves "when the perforator (and drug) has penetrated into the patient's body with body fluid and/or solvent in the drug reservoir." See, *e.g.*, abstract, lines 5-7; and ¶ 10, lines 1-9; and ¶ 20, lines 1-9. The Kwon publication indicates that "[t]he biodegradation or dissolution process may occur over a time interval of between a few tens of seconds and a few hours." See, *e.g.*, ¶ 20, lines 9-12. The composition of the matrix can control the release of the drug from the solid perforators; a faster dissolving matrix is used for high doses and a slower dissolving matrix is used for sustained drug release. See, *e.g.*, ¶ 54, lines 1-10. As such, the Kwon publication discloses a drug delivery device that administers a drug to the patient in a solid form by piecing the skin with solid perforators comprising the drug, an only after administration, is the drug subsequently released into the skin after the matrix comprising the perforators begins to degrade or dissolve.

The Applicant respectfully submits that the Kwon reference does not read on the presently claimed methods because this reference discloses a device that administers a solid form composition comprising a drug and not a liquid solution as presently claimed. The Kwon publication clearly teaches that the matrix and drug are mixed together as solids and that this mixture is then compressed into a perforator. See, *e.g.*, ¶¶ 25-32. At the time of administration the solid perforators are applied to the skin. It is only after subsequent exposure to bodily fluids or a solvent in a reservoir is the matrix material degraded or dissolved and the drug subsequently released into the body. Furthermore, the Kwon publication cannot inherently anticipate the presently claimed methods because at the time of administration, the perforators must be in a solid form in order to pierce the skin. Perforators as a liquid solution not only go against the clear teaching of the Kwon publication, but would, in fact, render the SSP device inoperable because liquid perforators would be incapable of piercing the skin.

The Examiner indicated that "there is no material difference between that which has been claimed and that of the prior art." March 22, 2007 Office Action at pg. 3, ¶ 2, lines 1-2. However, this is merely a conclusory statement unsupported by any factual finding. The Examiner has not cited any evidence nor provided a line of reasoning supporting the claim of no material difference. In addition, the Applicants respectfully point out that there is a definite material difference between administering a drug in a solid form versus a liquid solution. One

such material difference is that drugs administered using a SSP device allow for a controlled-release of the drug. See, *e.g.*, ¶ 9, lines 1-5; and ¶ 44, lines 1-5. A liquid solution is a one time administration that cannot control the release of a drug over time. Another material difference is that a using a SSP device provides prompt cut-off of drug delivery by removal of the device. See, *e.g.*, ¶ 24, lines 1-3. Once a liquid solution enters a body it cannot be removed. As such, the Examiner has not made a *prima facie* case of anticipation because the Examiner has not made of record any evidence or line of reasoning refuting the Applicant's position that the Kwon publication does not disclose the use of any liquid drug and the devices disclosed by Kwon are all limited to devices which use a solid drug.

In addition, the Examiner's contends that the Kwon publication "discloses the use of [botulinum toxin type A], which evidenced by Allergan [therapeutic insert], necessarily has been reconstituted because [botulinum toxin type A] is shipped as a sterile, vacuum-dried purified botulinum toxin type A." Assuming that this statement is true, it has no bearing to the question of whether a device comprising solid perforators containing a botulinum toxin anticipates administration of a liquid solution comprising a botulinum toxin type A as presently claimed. The issue is at the time of administration to the patient, what is the form of the composition comprising the botulinum toxin type A. The Kwon publication discloses a device that administers a botulinum toxin type A in a solid form. The presently claimed method administers a botulinum toxin type A in a liquid solution. Regardless of how a botulinum toxin type A was shipped, a person of ordinary skill in the art wishing to use the device disclosed in the Kwon publication would have to process this toxin using the proceeds taught at ¶¶ 25-32 in order to make a SSP device comprising solid perforators containing a dissolvable matrix and the toxin. Likewise, a person of ordinary skill in the art wishing to administer a liquid solution comprising a botulinum toxin type A as presently claimed would have to reconstitute the toxin using water or saline as taught at, *e.g.*, pg. 11, lines 16-30 and pg. 32, lines 14-17. Thus, the Examiners contention does not provide any evidence establishing that the Kwon publication anticipates the presently claimed methods.

Thus, the Applicant respectfully submits that the Examiner has not established a *prima facie* case of anticipation because no evidence or line of reasoning relevant to this issue has been

made of record. Therefore, the Applicant respectfully requests withdrawal of the 35 U.S.C. §102(b) anticipation rejection for Claims 1-5 and 12.

II. The Kwon publication does not disclose administering by intradermal or subdermal injection or by topical cream or lotion.

As discussed above, administration of a botulinum toxin of the presently claimed methods involves either 1) an intradermal or subdermal injection; or 2) topical administration of a cream or lotion. As discussed above, the Kwon publication discloses a drug delivery device that administers a drug to the patient in a solid form by piecing the skin with solid perforators comprising the drug, and only after administration, is the drug subsequently released into the skin after the matrix comprising the perforators begins to degrade or dissolve. The Kwon reference states that "[i]n contrast to conventional hollow needle technologies, the SSP system includes a solid matrix of dissolvable (including meltable) or biodegradable material that optionally holds one or more selected drugs and is formed into one or more perforators." See, *e.g.*, ¶ 11, lines 1-5. Because the SSP device comprises solid perforators, it is neither capable of injecting a liquid solution or being applied as a cream or lotion. As such, the Kwon publication does not read on the presently claimed methods because it does not administer a botulinum toxin using an intradermal or subdermal injection or a topical cream or lotion. Therefore, the Applicant respectfully submits that the pending claims are not anticipated by the Kwon publication and respectfully request withdrawal of the 35 U.S.C. §102(b) anticipation rejection for Claims 1-5 and 12.

Rejection Pursuant to 35 U.S.C. § 112, ¶ 1 New Matter Rejection

The Examiner has rejected Claims 13-16 as allegedly lacking written description support under 35 U.S.C. § 112, ¶1 because the phrase "the step of administering a therapeutically effective amount of a reconstituted liquid solution of botulinum toxin via syringe to a location of a skin disorder of the patient" does not appear in the present specification or claims as originally filed and thus is considered a new matter. The Applicant respectfully asks for reconsideration under 37 C.F.R. §1.111.

Although the Applicants disagree with the Examiner, the amendment of Claims 13-16 for reasons having nothing to do with this new matter rejection, render this rejection immaterial. As such, the Applicant respectfully requests withdrawal of the 35 U.S.C. § 112, ¶1 written description rejection against Claims 13-16.

Rejection Pursuant to 35 U.S.C. § 103(a) Obviousness

The Examiner has rejected Claims 6 and 8-10 as allegedly being obvious pursuant to 35 U.S.C. § 103(a) over the Kwon publication. The Examiner contends that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify the SSP device of the Kwon reference to create the presently claimed methods because the Kwon publication discloses a method of administering botulinum toxin type A for "treating lesions or abnormal skin features, such as pimples, corns, warts, calluses, bunions and keratoses." March 22, 2007 Office Action at pg. 5, point 5, ¶ 3, line 1 through pg. 6, point 5, ¶ 1, line 1. The Applicant respectfully asks for reconsideration under 37 C.F.R. §1.111.

I. Kwon teaches away from the presently claimed methods.

According to MPEP §2143.03, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. The Applicants respectfully submit that it would not be obvious to modify the Kwon publication because this publication teaches away from a method of treating a skin disorder by administering a liquid solution comprising a botulinum toxin by an intradermal or subdermal injection as presently claimed.

As discussed above, the Kwon publication discloses a drug delivery device that administers a drug to the patient in a solid form by piecing the skin with solid perforators composed of a matrix material and the drug. The Kwon reference states that "[i]n contrast to conventional hollow needle technologies, the SSP system includes a solid matrix of dissolvable (including meltable) or biodegradable material that optionally holds one or more selected drugs and is formed into one or more perforators." See, *e.g.*, ¶ 11, lines 1-5. Since the SSP device comprises solid perforators, it is not capable of injecting a liquid solution. As discussed able,

the drug is a component of the perforator, thus at the time of administration, the drug is necessarily solid because the perforator must be solid in order to pierce the skin.

Thus, the Kwon publication teaches a SSP device that administers a drug in a solid form via perforators, and not as a liquid solution and that such perforators must be in solid form at the time of administration in order to pierce the skin. Therefore, the Applicants respectfully submit that a *prima facie* case of obviousness cannot be made because the teaching of the Kwon publication teaches away from a method of treating a skin disorder by administering a liquid solution comprising a botulinum toxin by intradermal or subdermal injection or by topical administration using a cream or lotion.

II. Modification of Kwon makes it unsatisfactory for its intended use.

According to *MPEP* § 2143.01, "if proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." Citing In re Gordon, 733 F.2d 900, 902 (Fed. Cir. 1984). The Applicants respectfully submit that it would not be obvious for one of ordinary skill in the art to modify the Kwon publication because such modification would render the SSP device disclosed in the Kwon publication inoperable for its intended use.

As discussed above, the Kwon publication discloses a drug delivery device comprising solid perforators composed of a matrix material and a drug where the perforators are capable of piercing the skin. The ability to pierce the skin is clearly a critical feature of the SSP device since the Kwon publication indicates that "[a]s long as an SSP perforator dissolves reasonably quickly and is strong enough to pierce the stratum corneum, any biocompatible material can serve as an SSP perforator" See, *e.g.*, 24, lines 5-8. Modifying the solid perforators into a liquid solution would render the SSP device inoperable because it would no longer be strong enough to pierce the stratum corneum.

Thus, the Applicants respectfully submit that a *prima facie* case of obviousness cannot be made because modification of the Kwon publication as suggested by the Examiner would result in a SSP device that would be inoperable for its intended purpose.

III. Kwon provides no motivation to modify.

According to *MPEP* § 2143.01, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the references also suggests the desirability of the combination. The Applicants respectfully submit that it would not be obvious for one of ordinary skill in the art to modify the Kwon reference because there would be no desirability to make the proposed modification.

As discussed above, the Kwon publication discloses a drug delivery device comprising solid perforators composed of a matrix material and a drug where the perforators are capable of piercing the skin. Release of the drug contained in the solid perforators are released by diffusion once the matrix begins to degrade or dissolve. The biodegradability or dissolvability of the solid perforators is clearly an important feature of the SSP device since the Kwon publication indicates that "[a]s long as an SSP perforator dissolves reasonably quickly and is strong enough to pierce the stratum corneum, any biocompatible material can serve as an SSP perforator" See, *e.g.*, 24, lines 5-8. As such, the Kwon reference neither directly or implicitly teaches or suggests the delivery of a drug by injection.

CONCLUSION

For the above reasons the Applicants respectfully submit that the claims are in condition for allowance, and the Applicants respectfully urge the Examiner to issue a Notice to that effect. Should there be any questions, the Examiner is invited to call the undersigned agent.

Please use Deposit Account 01-0885 for the payment of any extension of time fees pursuant to 37 C.F.R. § 1.136 or any other fees due in connection with the current response.

Respectfully submitted,

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